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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
08/796,040	02/05/97	COLPAN	M P58126US1

EXAMINER

12M1/0624

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ART UNIT	PAPER NUMBER
1211	24

DATE MAILED: 06/24/97

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 02/05/97, Amdts E & F, papers no.s 22 & 23

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 62-80 is/are pending in the application.
Of the above, claim(s) _____ is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☒ Claim(s) 62-80 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

[x] Claims 1-61 have been cancelled.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☒ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☒ received in Application No. (Series Code/Serial Number) 08/244,530 (PCT application copy only)
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: Fed Rep. Germany 4139664.2

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of Reference Cited, PTO-892
☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
☐ Interview Summary, PTO-413
☒ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

SN 08/796,040 **--SEE OFFICE ACTION ON THE FOLLOWING PAGES--**

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group 1200, Art Unit 1211.

Claims **40-61** have been cancelled and claims **62-80** have been added per the amendments filed February 5, 1997.

Claims **62-80** remain in the case.

35 U.S.C. §101 reads as follows:

> "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title."

Applicant is requested to note that claims **62** (both occurrences of "using"), **65, 67 and 68** violate both 35 U.S.C. §101 and 35 U.S.C. §112 since they are each drafted in terms of "use." See *Clinical Products v. Brenner*, 255 F. Supp. 151, 149 USPQ 475 (1966). In the noted claims the term "using" is deemed to be the equivalent of the term "use."

Claims **62-80** are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim **62**, lines 1-2. the term "in particular, plasmid or genomic DNA," is indefinite. Applicant may chose to more narrowly specify the claimed subject matter by introduction of dependent

claims.

In claim **69**, the term "wherein the ionic exchanger has a high surface charge" begs the question --How high?--, and also suggests that applicant has not completely defined the subject matter being claimed.

Claim **64** lacks proper antecedent basis in claim **62** as the subject matter to which this claim is directed is absent from claim **62**.

In claims **72-73 and 79-80** the term "includes" is incorrect as applied to a compound as said term is used as the equivalent of open language , e.g. --comprises--. Applicant is requested to note that claims directed to chemical compounds are indefinite when terms using variations of the verb "to comprise" or their verbal equivalents are included, because consequently said terms imply the presence of other component parts which are not defined in the instant claims; e.g. metes and bounds are indeterminant. In claim **79**, at line 3, in particular, the structure of the claim is also made indefinite by the symbol "/" and the term "of a mixture thereof." It is unclear what combinations of solutes and cosolvents applicant is actually claiming. The same problem occurs in claims **70 and 80** wherein the terms "comprises from 10 to 100,000 nucleotides" and "comprises water and Tris", respectively, are found indefinite for failure to further define the implied missing components of the nucleotide and the buffer, respectively.

Claims **71 and 79** are rejected under 35 U.S.C. §112, first paragraph, as the disclosure is enabling only for claims wherein the scope of the claimed subject matter is commensurate in scope with

disclosed specific embodiments directed to nucleic acid purifications using a single adsorbant only and where alcoholic precipitating solutions do not contain more than three components. See MPEP 706.03(n) and 706.03(z).

In claims **71 and 79**, the term "or a combination thereof" and "or a mixture thereof", respectively, are lacking in proper enablement as no teachings are found which disclose how to use either any single mixture of adsorbants or any more than one of the vast array of pH adjusted binary and ternary mixtures of ionic solutes and cosolvents being claimed when practicing the claimed invention. The use of higher order pH adjusted solvent/solute mixtures is not taught herein in any specific embodiment.

The disclosure is objected to because of the following informalities:

At p. 21, Example 3, line 8, reference is made to "Example 3", the same example as is being delineated. Did applicant intend to refer to an earlier example and if so which one?.

At pp. 21-22, Example 4, reference is made to the addition of "saponin" and "proteinase K" to cause cell lysis. How can applicant then subsequently refer to whole cells being trapped and subsequently lysed by "Tween," unless cells are being reassembled ("magic wand" in there somewhere?)?

Appropriate correction is required.

The following is a quotation of 35 U.S.C. §103 which forms the basis for all obviousness rejections set forth in this Office action:

"A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person."

Claims **62-80** are rejected under 35 U.S.C. §103 as being unpatentable over Henco et al. '426 in combination with Little '430.

The instant claims are directed to a process for DNA purification with the following steps:
i) cell lysis using an enzyme (e.g. Rnase A) or using a mixture of chemical reagents (e.g. buffered SDS) and debris removal using filtration and/or centrifugation;
ii) contacting the filtrate from step i) with an anion exchange resin in buffers of low ionic strength, and elution of the DNA from the anion exchange resin by contacting with a high-ionic-strength buffer, optionally following the addition of a lower alcohol, or of polyethylene glycol, and
iv) desalting the DNA-containing solution by contacting same with a mineral support material to effect adsorption of the DNA onto the mineral support material (e.g silica gel) followed by washing the adsorbed DNA with alcoholic solutions to remove salts, and elution of DNA from the mineral adsorbant by contacting the mineral support

material with a low ionic strength buffer (e.g. buffered Tris) or with water.

Henco et al. '426 discloses a four step process summarized as follows:

i) cell lysis/filtration by any one of numerous known methods including the use of detergents, proteolytic enzymes or mechanical procedures (see claim 8) including centrifugation (see column 6, lines 51-66);

ii) anion exchange chromatography by transferring the product solution from step i) to an anion exchange resin followed by washing with a low ionic strength buffer the intended effect of which is to remove all of the interfering substances (e.g. RNA, proteins) from long chain DNA which remains adsorbed on the column optionally in the presence of known DNA precipitants polyethylene glycol or isopropanol (see col. 12, lines 41-42);

iii) elution of the long chain DNA from the anion exchange column adsorbant with high ionic strength buffer; and

iv) desalting the DNA by one of several different methods. One method of desalting not mentioned in the Henco disclosure is adsorption chromatography wherein a sample of DNA is applied to the column adsorbant such as silica gel in the presence of a high ionic strength buffer and separated therefrom by subsequent elution with low ionic strength buffer or water alone.

Little '430 at column 7, lines 12-45, discloses one of several examples wherein DNA is extracted from cells of various types using chaotropic ion/enzyme-mediated digestion followed by centrifugation and ultimately chromatographic separation using a commercial diatomaceous earth (Celite™) and various buffer solutions. As noted

in the abstract, Little discloses the application of DNA to the adsorbant from a relative high ionic strength solution, washing to remove salts, and subsequent elution of the adsorbed DNA with a low ionic strength buffer or with water. This reference does not disclose the use of anion exchange resins to selectively retain DNA in a purification process.

Applicant's combination of,
a) conventional cell lysis,
b) the physical separation of cell debris,
c) the anionic exchange chromatography of the filtrate isolated from the cell debris, and
d) finally desalting of the DNA-containing eluate form the anion exchange column by application to a chromatographic adsorbant (e.g. silica gel) to effect the desalting,

is a combination of process steps well known in the prior art and motivated generically by the disclosures of Henco et al. '426, with specific desalting step details disclosed by the Little '430 reference. As noted supra, Henco does teach the use of DNA desalting subsequent to anion exchange. The failure to teach the specific desalting method of the instant claimed method by Henco '426 has been addressed in the instant rejection of record by combining with the Little '430 reference, which discloses the utility of classical chromatography adsorbants for the purpose of isolating purified DNA in solutions with low net ionic strength. For this reason applicant's claimed process has been found to be nothing more than a combination of the Henco reference with Little et al.'430, wherein Henco provides the motivation to combine by noting the need to desalt the high-ionic-strength solution of DNA produced by anion exchange chromatography (see column 7, lines 44-46; or col. 12, lines 42-43).

The specific details of washing steps, the timing of steps, the specific selection of wash solution contents, and the physical characteristics of the anion exchange resin and mineral adsorbant (e.g., particle diameter, pore size, etc.) are deemed to be variables clearly within the perview of the ordinary practitioner seeking to optimize the Henco and Little process steps for a specific situation. Therefore, the details of adsorbant choice, or other standard performance parameters (e.g. the frequency of washes, the variation of ionic strength in wash solutions, etc.) are deemed to be the kind of variables properly within the realm of routine experimentation by an ordinary practitioner in the course of optimizing the process steps disclosed in the prior art of record. For these reasons, the instant claims, in so far as they are directed to routine changes in experimental details of the kind noted above, are deemed to lack an adequate basis for a finding of patentable distinction for any variation of the instant claimed process, as such variations are deemed to have been properly included within the scope of the noted prior art.

Therefore, the instant claimed process for DNA purification by anion exchange chromatography followed by desalting using an entirely conventional adsorption chromatographic process would have been obvious to one of ordinary skill in the art having the above cited references before him at the time the invention was made.

Papers related to this application may be submitted to Group 1200 via facsimile transmission(FAX). The transmission of such papers must conform with the notice published in the Official Gazette (1096 OG 30, November 15, 1989). The telephone numbers for the FAX machines operated by Group 1200 are **(703) 308-4556 (for Official papers)** and **703-308-7923** (for Draft communications).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner L. E. Crane whose telephone number is 703-**308-4639**. The examiner can normally be reached between 9:30 AM and 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John Kight III, can be reached at (703)-308-1235.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1200 receptionist whose telephone number is 703-**308-1235**.

LECrane:lec
6/21/97

L. Eric Crane
Patent Examiner
Group 1200